REMARKS

Applicant's attorney wishes to thank the Examiner for the careful consideration given to this case. In order to better define the invention and distinguish over the prior art, claims 33 - 66 are now presented. These claims are briefly discussed below in order of numerical sequence.

Claims 33 - 42 and 63 - 66 relate to the use of ultrasound during chromatography, i.e. when a process liquid containing components to be separated is passed through the bed for separation. During such processing, the ultrasound transmissions have been found capable of identifying the passage of bands of separated component through the bed, leading to advantages in monitoring and controlling chromatography. The progression of bound impurities may also be detected.

Claims 43 - 48 relate to the use of ultrasound to determine "bed properties" such as density and compression in the mass of media particles.

Claims 49 - 62 relate to the packing of the column, that is, the procedure for filling it with a bed of particulate medium which is then used in chromatography. The use of ultrasound in accordance with the invention may enhance the packing procedure and make it easier to control or automate.

The packing of the bed and the properties of the packed bed are particularly described in connection with FIGS. 1 - 10 and 15 - 18 of the drawings. The separation

of components and the monitoring of bound impurities are described in connection with FIGS. 11 - 14 and 19.

It should be appreciated that ultrasound is used in accordance with the claims to detect the presence of packed bed particles during packing as opposed to the absence of the same. In comparison, during separation processing, ultrasound is used to detect the more subtle phenomena of small amounts of chemical substances transiently present in some part of the packed bed. Accordingly, as reflected in the claims, applicant has discovered that ultrasound may be used in the detection and monitoring of various characteristics of the packed bed during its formation and operation.

It is respectfully requested that the Examiner reconsider and withdraw the rejection of the claims under 35 USC 102(b) as anticipated by or, in the alternative, under 35 USC 103(a) as obvious over GB Patent No. 1,312,096 to Miller. As discussed below, Miller's use of a sonic probe in relation to the particle bed column is distinguished from the claimed use of ultrasound to identify the progress of bands of separated components through the bed, bed properties and presence of packed bed particles in the packing of the column.

Initially, it is noted that the Miller column is not a chromatography column. The column functions to separate mixed particles of different densities using an up-flow of liquid. The particles are of a type that may be used in chromatography, namely ion exchange resins,

but the analogous chemical process (e.g. water treatment, not chromatography) takes place in a different column. The Miller illustrated column is only for separating two different kinds of ion exchange resins after they have been exhausted. The Miller column is not filled with a packed bed. Contrarily, its action depends on maintaining turbulence and mixing of the spent particles. The purpose of the sonic probe 50 is quite different from that of the present invention. In Miller, the probe is only used to detect whether the top of the mass of particles in the column is at the proper level. This is a known use of ultrasound in processing vessels, and it is acknowledged in the present application at page 19, lines 15 - 20.

Accordingly, Miller fails to disclose or suggest the monitoring of the progressive advance of a bed surface up the column towards a fully-packed condition. Rather, the aim in Miller is to maintain a constant level. Further, it is also emphasized that the bed of particles in Miller is continually being changed because the particles are themselves the material being processed in the column.

In addition to the chromatography column environment of the present claims, as contrasted with the Miller disclosure, it is also emphasized that the recited process steps distinguish from the non-chromatography process in Miller. For example, claim 33 clearly specifies passing a process liquid for separation through a packed bed in the column to separate its components

chromatographically. This step does not take place in Miller, and it is not suggested since Miller is not doing chromatography in his column.

With regard to claims 49 - 62, it is emphasized that these claims specify a procedure in which a bed of medium gradually accumulates in a column and ultrasound signals are used to monitor the advance of the bed front and control the advance using feedback. Miller does not describe or suggest the monitoring of an advancing bed front. Further, claim 49 also recites performing a chromatography step in the columns using the bed which has been packed.

It is also emphasized that Miller does not teach or suggest the use of ultrasound to monitor the bed properties as set forth in claims 43 - 48. There is no motivation to monitor the Miller bed for such properties.

For the reasons set forth above, it is further submitted that the claims are not rendered obvious under 35 USC 103(a) as unpatentable over Miller in view of U.S. Patent 4,324,131 to Rosencwaig. The use of ultrasound in Rosencwaig is not pertinent to the processes now defined by the claims. More particularly, Rosencwaig teaches the use of ultrasound to detect dissolved substances in a liquid coming off his column. In this regard, the patentee notes that ultrasound may provide a useful detector for dissolved substances.

Accordingly, Rosencwaig does not suggest or render obvious the processes set forth in the claims presently

of record. Rosencwaig applies his ultrasound transmissions to liquid alone in a flow cell, relying on comparison with an adjacent reference cell containing the corresponding solvent without solute, in order to obtain a result. This is not suggestive of the claimed use of passing an ultrasound signal through a bed of packed solid particles in a chromatography column in order to detect the presence of a band of eluting component actually in the column in the form of a substance that is substantially adsorbed on the bed particles. The Rosencwaig teaching is, therefore, not useful to modify Miller in order to meet the claimed invention. Further, there is no motivation in the prior art for any pertinent combination of their teachings to meet or suggest the subject matter of claims 33 - 42 and 63 - 66.

The use of ultrasound to detect such a band of eluting component is truly remarkable and distinguished from the prior art. The monitoring of eluting components while they are still in the column is of significant value to the practitioner in this field, especially when compared to the conventional monitoring of components only after they have left the column. Rosencwaig has no relevance to claims 49 - 62 which relate to the packing of the column. Similarly, Rosencwaig provides no meaningful suggestion of the use of ultrasound to determine bed properties as defined in claims 43 - 48.

For all of the same reasons set forth above, it is further urged that the claims presently of record are not

rendered obvious under 35 USC 103(a) as unpatentable over Miller in view of U.S. Patent 5,061,371 to Tabata. Tabata is specifically cited in connection with the use of a plurality of monitoring locations. As discussed below, the multiple monitoring locations in Tabata do not suggest the claimed process.

In Tabata, the column is only partially filled with particles and a layer of free liquid lies on top of the particle bed. The depth of the layer of liquid depends on the relationship between the inlet flow rate of process liquid and eluent through the process inlet 13, the outlet flow rate of process liquid through the discharge piping 14 and the height of the packed bed which varies due to its expansion during the process. The Tabata apparatus deals with these variations by using top detector 5 to monitor the height of the liquid surface and side detectors 18 to monitor the approximate height of the particle bed surface. The depth of the liquid layer is checked by comparing these values and, if it does not match the target value it is varied by adjusting the rate of inflow and/or outflow of the process using flow controllers 6, 7.

Tabata does not teach the packing of the particulate bed, and there is no suggestion that it would or could have been done through a packing port. (Column 3, lines 8 - 25.) Packing by injection through a packing port was essentially unknown in 1990.

In Tabata, the detectors 18 are installed down the sidewall of the column. These are to detect the height of the interface between the particle bed surface and the liquid layer above. According to column 3, lines 63+, such detectors 18 "may be of any of a vibrator type, a photoelectric tube type, a laser type, and the like, among which the vibrator type level sensor is preferred with respect to being simple in handling". On the other hand, the liquid level detecting element 17 provided at the top of the column is directed downwardly to determine the level of the liquid surface. The detector 17 may be ultrasound, as indicated at column 3, lines 45 - 50. Thus, Tabata does not disclose a plurality of detectors in connection with ultrasound monitoring of a column.

It should be appreciated that a vibratory sensor is a term of art, and refers to something different from an ultrasound transducer. The vibratory sensor is necessarily an invasive component that detects the presence of a material around the probe by direct mechanical interaction with it, transmitting vibrations between closely adjacent "prongs".

Accordingly, the only use proposed in Tabata for ultrasound is to detect the liquid level. Again, this is a conventional use of ultrasound that has no relation to the claimed process as set forth in the claims. Particularly, Tabata provides no suggestion that transmitting ultrasound through a packed bed provides useful information about the internal bed condition, in

particular, how densely the bed is packed and whether other materials such as contaminants or eluting product components are present in the bed.

The process set forth in claims 49 - 62 are also further distinguished from Tabata. Claim 49 specifies the use of an ultrasound arrangement during the packing of the column, whereas Tabata relates only to the chromatography step. Further, Tabata relates specifically to a process/apparatus, in which the column is not entirely filled with packing medium as compared with the claimed process which relates expressly to columns that are filled with packing medium as particularly set forth in the fourth line of claim 49. (Specification, page 1, lines 20-23.)

It should also be appreciated that there is no analogy between the process set forth in claims 49 - 62 and that contained in Tabata. The claimed process relates to the improved packing before chromatography, and the Tabata process relates to the maintenance of a constant depth of liquid above a particle bed during chromatography.

For all of the foregoing reasons, it is respectfully submitted that all of the claims presently of record are in condition for final allowance an such action is requested.

If there are any further fees required by this amendment not covered by the enclosed check, or if no

check is enclosed, please charge the same to Deposit Account No. 16-0820, Order No. 34516.

Respectfully submitted,

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